I(WE) CLAIM:

1. A method to identify an agent that alters UBP43 activity comprising:

(a) contacting a test cell with a candidate agent;

(b) determining the amount of an ISG-conjugate in the test cell;

(c) determining the amount of the ISG-conjugate in a control cell, wherein the control cell is not contacted with the candidate agent; and

(d) comparing the amount of ISG15-conjugate in the test cell to the amount of ISG15-conjugate in the control cell, wherein a difference in the amount of ISG15-conjugate indicates that the agent alters UBP43 activity.

2. The method of claim 1, wherein the test cell, the control cell, or both of the test cell and the control cell express an interferon receptor.

3. The method of claim 2 further comprising contacting the test cell, the control cell, or both the test cell and the control cell with IFNα, IFNβ, double-stranded ribonucleic acid, or lipopolysaccharide.

4. The method of claim 1, wherein the test cell is a $UBP43^{+/+}$ cell, a $UBP43^{+/-}$ cell, or a $UBP43^{-/-}$ cell.

5. The method of claim 1, wherein the control cell is a $UBP43^{+/+}$ cell, a $UBP43^{+/-}$ cell, or a $UBP43^{-/-}$ cell.

6. The method of claim 1, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-ERK2, ISG15-Stat1, and a variant thereof.

7. A method to identify an agent that alters UBP43 activity comprising:

(a) contacting a composition comprising UBP43 and a substrate, with a candidate agent, wherein the substrate comprises a donor molecule and an acceptor molecule;

(b) determining the fluorescence resonance energy transfer between the donor molecule and the acceptor molecule in step (a); and

(c) determining the fluorescence resonance energy transfer between the donor molecule and the acceptor molecule in the composition comprising UBP43 and the substrate, without the candidate agent, wherein a difference in the fluorescence resonance energy transfer between the donor molecule and the acceptor molecule indicates that the agent alters UBP43 activity.

8. The method of claim 7, wherein the substrate comprises an ISG15-conjugate.

9. The method of claim 8, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISGI15-Jak1, ISG15-ERK1, ISG15-ERK2, ISG15-Stat1, and a variant thereof.

10. A method to identify an agent that inhibits UBP43 activity comprising:

(a) contacting a composition comprising UBP43, a substrate, with a candidate agent, wherein the substrate comprises a donor molecule and an acceptor molecule;

(b) determining the fluorescence resonance energy transfer between the donor molecule and the acceptor molecule in step (a); and

(c) determining the fluorescence resonance energy transfer between the donor molecule and the acceptor molecule in the composition comprising UBP43 and the substrate, without the candidate agent, wherein substantially no change in the fluorescence

resonance energy transfer between the donor molecule and the acceptor molecule indicates that the agent inhibits UBP43 activity.

11. The method of claim 10, wherein the substrate comprises an ISG15-conjugate.

12. The method of claim 11, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-ERK2, ISG15-Stat1, and a variant thereof.

13. A method to induce a cell to undergo apoptosis comprising contacting a cell with a composition comprising an ISG15-conjugate, and measuring the presence or amount of cellular apoptosis, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-Stat1, and a variant thereof.

14. The method of claim 13, further comprising contacting the cell with IFNα, IFNβ, double stranded ribonucleic acid, or lipopolysaccharide.

15. The method of claim 13, wherein the ISG15-conjugate cannot be cleaved by UBP43.

16. The method of claim 13, wherein the ISG15-conjugate includes a non-hydrolysable bond.

17. The method of claim 13, wherein the composition further comprises a pharmaceutically acceptable carrier.

18. The method of claim 13, wherein the composition is contained within a liposome.

19. A method to prolong or increase the response of a cell to interferon comprising contacting the cell with a composition comprising an ISG15-conjugate, contacting the cell with an interferon, and measuring the response of the cell to the interferon, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-Stat1, and a variant thereof.

20. The method of claim 19, wherein the ISG15-conjugate cannot be cleared by UBP43.

21. The method of claim 19, wherein the composition further comprises a pharmaceutically acceptable carrier.

22. The method of claim 19, wherein the composition is contained within a liposome.

23. The method of claim 19, further comprising contacting the cell with IFNα, IFNβ, double-stranded ribonucleic acid, or lipopolysaccharide.

24. A method to inhibit cell proliferation comprising contacting a cell with a composition comprising an ISG15-conjugate, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-Stat1, and a variant thereof.

25. The method of claim 24, wherein the composition further comprises a pharmaceutically acceptable carrier.

26. The method of claim 24, wherein the composition is contained within a liposome.

27. The method of claim 24, further comprising contacting the cell with an interferon, double-stranded ribonucleic acid, or lipopolysaccharide.

28. The method of claim 24, wherein the cell is a tumor cell.

29. A method to inhibit the infection or replication of a virus comprising contacting a cell exposed to the virus with a composition comprising an ISG15-conjugate, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-Stat1, and a variant thereof.

30. The method of claim 29, further comprising contacting the cell with an interferon, double-stranded ribonucleic acid, or lipopolysaccharide.

31. The method of claim 29, wherein the virus is selected from the group consisting of hepatitis B virus, hepatitis C virus, human immunodeficiency virus, Epstein-Barr virus, herpes virus, rhinovirus, picornavirus, lentivirus, cytomegalovirus, respiratory syncytial virus, and poxvirus.

32. A method to treat an autoimmune disease comprising administering to a patient in need thereof an effective amount of a composition comprising an ISG15-conjugate, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-ERK2, ISG15-Stat1, and a variant thereof.

33. The method of claim 35, wherein the autoimmune disease is multiple sclerosis.

34. The method of claim 35, further comprising administering to the patient an IFNα, IFNβ, double stranded ribonucleic acid, or lipopolysaccharide.

35. A method to increase the effectiveness of an anticancer therapeutic comprising administering to a patient in need thereof an effective amount of the anticancer therapeutic, and administering to the patient an effective amount of a composition comprising an ISG15-conjugate, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-ERK2, ISG15-Stat1, and a variant thereof.

36. The method of claim 32, wherein the anticancer therapeutic is a cancer vaccine.

37. The method of claim 32, further comprising administering to the patient an INFα, IFNβ, double-stranded ribonucleic acid, or lipopolysaccharide.

38. An ISG15-conjugate that cannot be cleaved by UBP43.

39. The ISG15-conjugate of claim 38, wherein the ISG15-conjugate includes a non-hydrolysable bond at the cleavage site used by UBP43.

40. The method of claim 38, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-ERK2, ISG15-Stat1, and a variant thereof.

41. A composition comprising an ISG15-conjugate contained within a liposome and a pharmaceutically acceptable carrier.

42. The composition of claim 41, wherein the ISG15-conjugate is selected from the group consisting of ISG15-phospholipase Cγ1, ISG15-Jak1, ISG15-ERK1, ISG15-ERK2, ISG15-Stat1, and a variant thereof.

43. The composition of claim 41 further comprising interferon, double-stranded ribonucleic acid, or lipopolysaccharide.

44. A method to increase phagocytic activity of a cell comprising contacting a cell with a composition comprising an ISG15-conjugate.

45. A method to increase cell motility comprising contacting a cell with a composition comprising an ISG15-conjugate.

46. A method to enhance wound healing comprising contacting the wound with a composition comprising an ISG15-conjugate.

47. A method to promote or increase apoptosis in a cell comprising contacting the cell with a composition comprising an agent that inhibits UBP43 activity.

48. A method to prolong or increase the response of a cell to interferon comprising contacting the cell with a composition comprising an agent that inhibits UBP43 activity, contacting the cell with an interferon.

49. A method to inhibit the infection or replication of a virus comprising contacting a cell exposed to the virus with a composition comprising an agent that inhibits UBP43 activity.

50. A method to treat an autoimmune disease comprising administering to a patient in need thereof an effective amount of a composition comprising an agent that inhibits UBP43 activity.

51. A method to increase the effectiveness of an anticancer therapeutic comprising administering to a patient in need thereof an effective amount of the anticancer therapeutic, and administering to the patient an effective amount of a composition comprising an agent that inhibits UBP43 activity.

52. A method to increase phagocytic activity of a cell comprising contacting a cell with a composition comprising an agent that inhibits UBP43 activity.

53. A method to increase cell motility comprising contacting a cell with a composition comprising an agent that inhibits UBP43 activity.

54. A method to enhance wound healing comprising contacting the wound with a composition comprising an agent that inhibits UBP43 activity.